The Effect of Thyroid-feeding and of Thyro-parathyroidectomy upon the Pituitrin Content of the Posterior Lobe of the Pituitary, the Cerebro-spinal Fluid, and Blood.

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The material used for this research was obtained from cats. There were three series of six animals, comprising three males and three females in each group. The animals were healthy adults, of as near a weight and age as possible. One set of six animals was fed with large quantities of fresh ox thyroid for from two to three weeks in addition to their ordinary diet. In the second set thyro-parathyroidectomy was performed on each animal. The cats of the third group were utilised as normal controls. The feeding with thyroid of the first group was begun some time before the operations were done upon the second group. All the animals operated upon showed typical symptoms, and were killed from three to six days after operation. The cerebro-spinal fluid was collected from the fourth ventricle of each cat under anæthesia, the animal then bled, and the blood defibrinated. The pituitary body was dissected out and the posterior lobe separated and dried on a watch-glass rapidly at 37° C. The cerebro-spinal fluid was also evaporated and dried at the same temperature. Similar procedures were adopted in the thyroid-fed animals and in the controls.

In this way there were collected three materials—dried posterior lobe of pituitary, dried cerebro-spinal fluid, and defibrinated blood—from three groups of animals—normal, thyroid-fed, and thyro-parathyroidectomised cats. The materials were then tested physiologically—by Dale's method upon the uterus of the virgin rat, by Elliott's method upon the blood pressure of a pithed cat, and by their action upon the blood pressure, kidney volume, and secretion of an anæsthetised cat.

The Posterior Lobe of the Pituitary Body.

The amount of dried posterior lobe of the pituitary was approximately the same in each group of animals. The material of each group was ground in a mortar, and solutions in Ringer's fluid made up of corresponding amounts in each case. A 0·001 per cent. extract of the dried gland was finally adopted as the standard strength for testing. This dilution of posterior lobe acts powerfully upon the rat's uterus.

No appreciable difference is obtained between the action of the material from the three groups of animals. Immersion of the uterus in each solution was limited to fifteen seconds, and both height and duration of contraction are the same in the normal, thyroid-fed, and parathyroidectomised material.

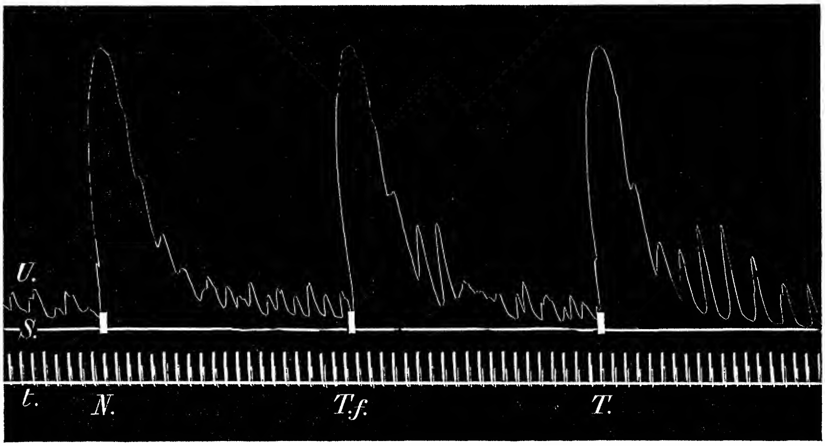

Fig. 1.—Effect upon the isolated uterus of the virgin rat of immersion in 0·001 per cent. extracts of dried pars nervosa of the pituitary body.
N., extract derived from normal cats; *T.f.*, extract from thyroid-fed cats; *T.*, extract from thyro-parathyroidectomised cats. The upper tracing: *U* represents the uterus; *S*, the signal; *t.*, the time in 30-second intervals.

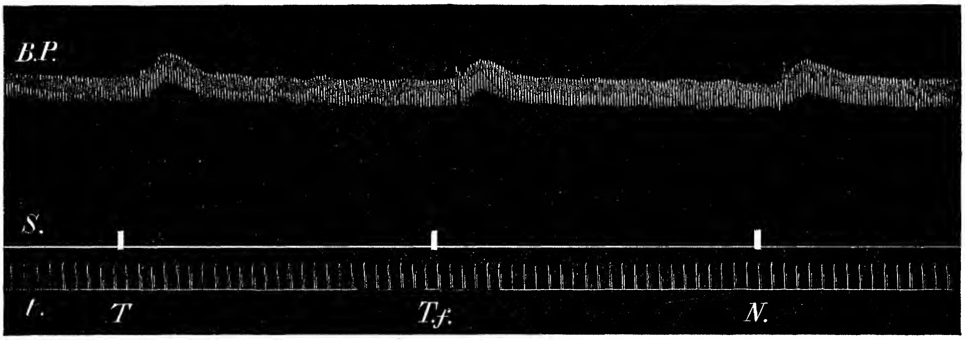

Fig. 2.—Effect upon the blood pressure of a pithed cat of the intravenous injection of 2 c.c. of a 0·001 per cent. extract of dried pars nervosa derived from
T., the pituitaries of thyro-parathyroidectomised cats; *T.f.*, the pituitaries of thyroid-fed cats; *N.*, the pituitaries of normal cats. *B.P.* is the carotid blood pressure; *S.*, the signal and zero line of blood pressure; *t.*, time in 10-second intervals.

When tested by Elliott's method upon the low blood pressure of a pithed cat, doses of 2 c.c. injected intravenously cause a small transient rise of blood pressure, but again no appreciable difference appears in the action of the three materials. The experiments were repeated and injections made in different orders, but no change in the results occurred.

It has been shown that the rat's uterus responds uniformly to the same extract of pituitary, and that the extent of the contraction varies directly with the strength of the extract employed[*]. The test is not sensitive to small differences, but a reduction in the strength of the solution of 50 per cent. yields an appreciable diminution in the extent of the uterine contraction. The blood pressure test in the pithed cat, which Elliott[†] showed to be very sensitive to minute amounts of adrenalin, is also a good method for revealing small differences in the strengths of weak solutions of pituitrin. With such minute doses, the action of pituitrin upon the circulation can be frequently repeated, and the depressor effect which usually results from a second injection, does not occur unless the first dose is a comparatively large one.

It is inferred, therefore, that there are no gross changes in the amount of pituitrin present in the posterior lobe of the pituitary body produced either by thyroid-feeding or by thyro-parathyroidectomy.

Cerebro-spinal Fluid.

The cerebro-spinal fluid from each series of animals yielded sufficient dried material to be made into three separate solutions of 1 per cent. each in Ringer's fluid. The extracts were tested upon the rat's uterus, and upon the blood pressure, kidney volume, and urinary secretion of an anæsthetised cat.

The extracts are practically inactive. A slight increase in the uterine contractions was observed after immersion of the uterus in the cerebro-spinal fluid of the thyro-parathyroidectomised cats, but was not a constant phenomenon. None of the extracts show any effect upon blood pressure, kidney volume, and urinary secretion other than that which is produced by a similar amount of Ringer's solution alone.

It would appear, therefore, that there is no appreciable amount of pituitrin in the cerebro-spinal fluid taken from the fourth ventricle, whether from normal, thyroid-fed, or thyro-parathyroidectomised cats. This does not exclude the possibility that pituitrin is occasionally liberated into the cerebro-spinal fluid in the third ventricle. If such takes place, one would expect rapid absorption to occur, and the probability is against the material reaching the fourth ventricle.

Carlson and Martin[‡] were unable to obtain any pressor effect from the cerebro-spinal fluid of normal dogs. Cushing and Goetsch,[§] on the other hand, found that in certain pathological conditions human cerebro-spinal fluid has the same action upon the blood pressure, kidney volume, and urinary secretion as extracts of the posterior lobe of the pituitary body.

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[*] Herring, 'Quart. Journ. Exper. Physiol.,' vol. 8, p. 268 (1914).

[†] Elliott, 'Journ. Physiol.,' vol. 44, p. 374 (1912).

[‡] Carlson and Martin, 'Amer. Journ. Physiol.,' vol. 29, p. 64 (1911).

[§] Cushing and Goetsch, 'Amer. Journ. Physiol.,' vol. 27, p. 60 (1910).

Defibrinated Blood.

The defibrinated blood shows little action upon the rat's uterus, and no appreciable difference is seen whether the blood be taken from the normal thyroid-fed, or thyro-parathyroidectomised animals.

When tested upon the blood pressure of an anæsthetised cat differences are at once revealed. The blood from the normal animals causes a distinct fall of arterial blood pressure accompanied by contraction of the kidneys and a slowing of urinary secretion. This is succeeded by a return to normal of the blood pressure, slight dilatation of the kidney and increased urinary secretion.

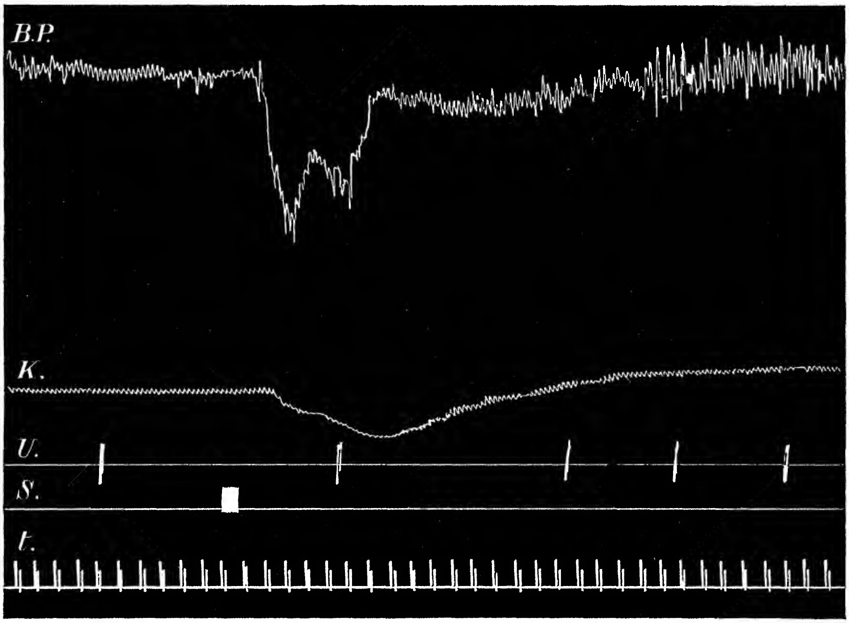

Fig. 3.—Effect upon blood pressure, kidney volume and urinary secretion (cat) of the intravenous injection of 3 c.c. of defibrinated blood of normal cats. *B.P.*, carotid artery blood pressure ; *K.*, kidney volume ; *U.*, urine drops ; *S.*, signal ; *t.*, time in 10-second intervals.

The blood from the thyroid-fed cats has a similar but more pronounced action, the blood pressure falls lower, indicating the presence in the blood of the thyroid-fed animal of more depressor material than is present in the normal animal.

The blood from the thyro-parathyroidectomised cats, on the other hand, shows a slight depressor action followed by a distinct pressor effect which lasts for some time. The kidney shows a transient contraction, and the flow of urine is distinctly diminished.

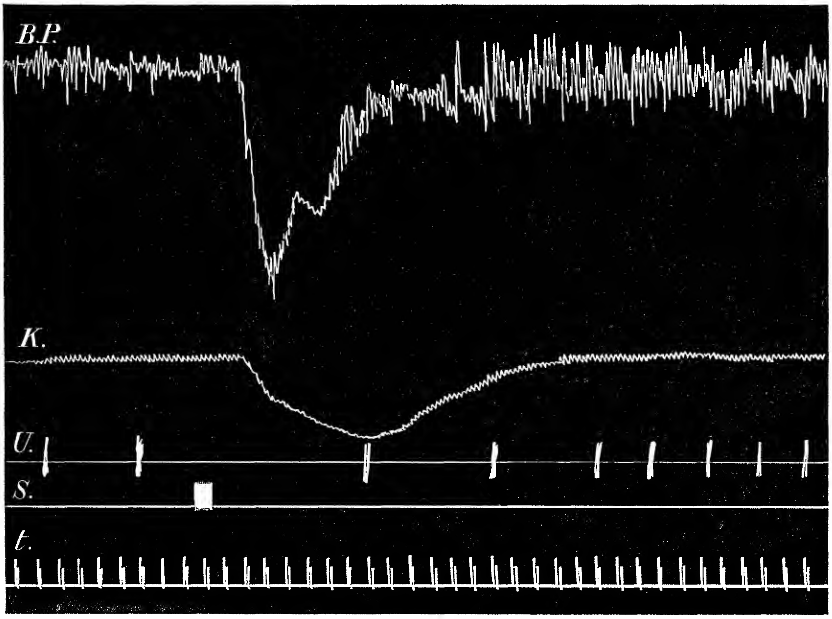

Fig. 4.—Effect upon blood pressure, kidney volume, and urinary secretion (cat) of the intravenous injection of 3 c.c. defibrinated blood of thyroid-fed cats.

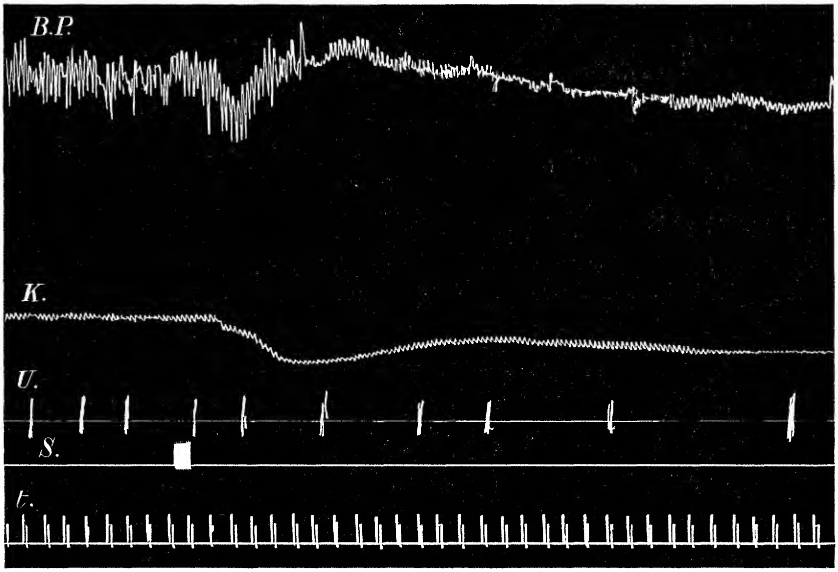

Fig. 5.—Effect upon blood pressure, kidney volume, and urinary secretion (cat) of the intravenous injection of 3 c.c. defibrinated blood of thyro-parathyroidectomised cats.

As the thyro-parathyroidectomised animals showed symptoms of tetany before death it is probable that the pressor action of their blood is due to the presence in it of guanidin, or allied bodies, as described by Noël Paton* and his co-workers.

Summary.

1. Neither thyroid feeding nor thyro-parathyroidectomy affects the pituitrin load of the posterior lobe of the pituitary body as tested by the action of extracts upon the contraction of the rat's uterus and the blood pressure of the pithed cat.

2. There is no evidence of the presence of pituitrin in the cerebrospinal fluid of the fourth ventricle in normal, thyroid-fed and thyro-parathyroidectomised cats.

3. The defibrinated blood of normal, thyroid-fed and thyro-parathyroidectomised cats shows no appreciable differences in its action upon the rat's uterus. The blood of the thyroid-fed cat has a greater depressor action upon the circulation than has that of the normal animal. The blood of the thyro-parathyroidectomised cat exercises a pressor effect upon the circulation, accompanied by a contraction of the kidney and a diminution in the secretion of urine.

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* Noël Paton, 'Quart. Journ. Exper. Physiol.,' vol. 10, p. 203 (1917).